cleavage site, and a unique SpeI restriction site that can be used for facile exchange of the antigen coding region. Example 2 below discusses the use of the equivalent peptide from Guinea pig, which has a serine in place of the threonine residue in the MBP-72-89 sequence. Figs. 1C (SEQ ID NO: 5-6) and Fig. 1D (SEQ ID NO: 7-8) show exemplary nucleotide sequences and their corresponding amino acid sequences of Nco1/SpeI fragments that can be inserted into the expression cassette in place of the MBP-72-89 antigen coding region. Fig. 1C includes the MBP-55-69 antigen, Fig. 1D includes the CM-2 antigen.

F1 Cont

*Please replace the paragraph on page 9, lines 18-21 with the following paragraph:*

Figs. 10A-C show the amino acid sequences of exemplary ß1 and α1 domains of (A) human (DRA and DRB1 0101) (SEQ ID NO: 22), (B) mouse ($I\text{-}E^K$) (SEQ ID NO: 23), and (C) rat (RT1.B) (SEQ ID NO: 24), respectively. The initiating methione and glycine sequences in the rat sequence were included in a construct for translation initiation reasons.

F2

*Please replace the paragraph on page 9, lines 22-23 with the following paragraph:*

Fig. 11 shows the amino acid sequence (SEQ ID NO: 21) of exemplary α1 and α2 domains derived from human MHC class I B*5301.

*Please replace the paragraph on page 10, lines 11-24 with the following paragraph:*

Fig. 13 is the nucleotide (SEQ ID NO: 43) and protein (SEQ ID NO: 44) sequence of human HLA-DR2-derived RTL303. RTL303 was derived from sequences encoding the beta-1 and alpha-1 domains of HLA-DR2 (human DRB1*1501/DRA*0101) and sequence encoding the human MBP85-99 peptide. Unique NcoI, SpeI and XhoI restriction sites are in **bold.** The end of the beta-1 domain and start of the alpha-1 domain are indicated by an arrow (▼). RTL303 contains an in-frame peptide/linker insertion encoding the human MBP85-99 peptide (**bold**), a flexible linker with an embedded thrombin cleavage site (23), and a unique SpeI restriction site which can be used for rapidly exchanging the encoded amino-terminal peptide. RTL301 is identical to RTL303 except for a single point mutation resulting in an F150L substitution. Two

F3

F3 Cont

additional proteins used in this study, RTL300 and RTL302, are "empty" versions of RTL301 and RTL303, respectively. These molecules lack the peptide/linker insertion (residues 16-115). Codon usage for glycines 32, and 51 have been changed from the native sequence for increased levels of protein expression in *E. coli* (G.G. Burrows, unpublished observations).

*Please replace the paragraph on page 14, lines 3-17 with the following paragraph:*

Fig. 25 is a set of graphs showing IL-10 cytokine production induced by RTL pre-treatment was maintained after stimulation with APC/peptide. T cells showed a reduced ability to proliferate and produce cytokines after anti-CD3 or RTL treatment, and the RTL effect was antigen and MHC specific. IL-10 was induced only by specific RTLs, and Il-10 production was maintained even after restimulation with APC/antigen. T cell clones were cultured at 50,000 cells/well with medium, anti-CD3, or 20 μM RTLs in triplicate for 48 hours, and washed once with RPMI. After the wash, irradiated (2500 rad) frozen autologous PBMC (150,000/well) plus peptide-Ag (MBP-85-99 at 10 μg/ml) were added and the cells incubated for 72 hr with $^{3}$H-thymidine added for the last 18 hr. Each experiment shown is representative of at least two independent experiments. Bars represent mean ± SEM. For cytokine assays, clones were cultured with 10 μg/ml anti-CD3 or 20 μM RTL303 or RTL311 for 48 hours, followed by washing with RPMI and re-stimulation with irradiated autologous PBMC (2500 rad, T:APC=1:4) plus peptide-Ag (10 μg/ml) for 72 hours. Cytokines (pg/ml) profiles were monitored by immunoassay (ELISA) of supernatants. Each experiment shown is representative of at least three independent experiments. Bars represent mean ± SEM.

F4

*Please replace the paragraph on page 15, line 10 with the following paragraph:*

F5 N.E.

SEQ ID NO: 28-31 are the nucleic acid sequences of primers used for human ß1α1.

*Please replace the paragraph on page 74, lines 5 - 27 with the following paragraph:*

Peptide-specific T cell clones were selected from peripheral blood mononuclear cells (PBMC) of a multiple sclerosis (MS) patient homozygous for HLA-DRB1*1501 and an MS patient homozygous for HLA-DRB1*07, as determined by standard serological methods and further confirmed by PCR amplification with sequence-specific primers (PCR-SSP) (Olerup et al., 1992). Frequencies of T cells specific for human MBP85-99 and CABL were determined by limiting dilution assay (LDA). PBMC were prepared by ficoll gradient centrifugation and cultured with 10 μg/ml of either MBP85-99 or CABL peptide at 50,000 PBMC/well of a 96-well U-bottomed plate plus 150,000 irradiated (2500 rad) PBMC/well as antigen-presenting cells (APCs) in 0.2 ml medium (RPMI 1640 with 1% human pooled AB serum, 2 mM L-glutamine, 1 mM sodium pyruvate, 100 μg/ml penicillin G, and 100 μg/ml streptomycin) for 5 days, followed by adding 5 ng/ml IL-2 (R & D Systems, Minneapolis, MN) twice per week. After three weeks, the culture plates were examined for cellular aggregation or "clump formation" by visual microscopy and the cells from the "best" 20-30 clump-forming wells among a total of 200 wells per each peptide Ag were expanded in 5 ng/ml IL-2 for another 1-2 weeks. These cells were evaluated for peptide specificity by the proliferation assay, in which 50,000 T cells/well (washed 3x) were incubated in triplicate with 150,000 freshly isolated and irradiated APC/well plus either medium alone, 10 mg/ml MBP85-99 or 10 mg/ml CABL pep- tide for three days, with $^{3}$H-Tdy added for the last 18 hours. Stimulation index (S.I.) was calculated by dividing the mean CPM of peptide-added wells by the mean CPM of the medium alone control wells. T cell isolates with the highest S.I. for a particular peptide antigen were selected and expanded in medium containing 5 ng/ml IL-2, with survival of 1-6 months, depending on the clone, without further stimulations.

F 6

## REMARKS

Pages 7, 9, 10, and 14 of the specification are amended herein to insert appropriate sequence identifiers for Figures 1A, 1B, 1C, 1D, 10A, 10B, 10C, 11, and 13, in order to comply